REMARKS

By this amendment, Applicants have amended claim 1 to include that the primer extension reaction is conducted in the presence of two or more labeled terminators. Claim 1 has also been amended to include that during separation, at least one detectable breakdown product and residual nucleotide terminator elutes before non-extended primers so as not to overlap in elution with primer extension product(s). Support for the amendments to claim 1 can be found in the specification, for example, at page 8, lines 20-32, page 9, lines 5-10, page 19, lines 20-29, page 24, lines 8-29, page 26, lines 20-21 and Example 1. New claim 15 has been added to include that after primer extension is conducted, separation is performed only once. New claim 16 has been added to include that the detection step is performed without further separation of breakdown products and residual labeled terminators from extended primer. Support for new claims 15 and 16 can be found in the specification, for example, at page 5, lines 14-24, page 8, lines 29-32 and Example 1. No new matter has been added. Applicants respectfully request entry of this amendment and allowance of the pending claims.

Rejection Under 35 U.S.C. § 102(e)

The Examiner rejected claims 1-5 and 7-14 under 35 U.S.C. §102(e) as allegedly being anticipated by Grossman U.S. Publication No. 2005/0112608 (Grossman '608). Applicants respectfully traverse this rejection.

To establish a *prima facie* case of anticipation under 35 U.S.C. §102(e) each and every element of the claims must be disclosed in the cited prior art reference. The present claims include, among other things, that after primer extension is conducted in the presence of two or more labeled terminators, detectable breakdown products and residual labeled nucleotide terminators are eluted before non-extended primers so as not to overlap in elution with primer extension product(s). Grossman '608 does not disclose this feature.

In the specification, Applicants describe that when labeled terminators are used in

the claimed sequencing method, detectable breakdown products from labeled terminators and residual (unincorporated) terminators result for various reasons (e.g., when high concentrations of labeled terminators or low concentrations of primer or template are used in the primer extension reaction). See, for example, page 5, lines 7-18 and page 8, lines 20-29. These breakdown products and residual terminators distort sequence data by causing interfering signals with labeled primer extension products when they are eluted.

By using a primer that contains a mobility-reducing moiety, interference from overlapping residual labeled terminators and terminator breakdown products is reduced or eliminated because the residual terminators and terminator breakdown products elute ahead of extended primers. This allows a more accurate detection of primer extension products, especially for primers that have been extended by one or two bases, which would otherwise co-migrate with detectable breakdown products or residual labeled terminators that emit the interfering signals.

Grossman '608 does not recognize the problem caused by interfering signals between labeled primer extension products and detectable breakdown products and residual labeled terminator nucleotides. In fact, Grossman '608 does not mention detectable breakdown products and residual labeled terminator nucleotides at all. Accordingly, Grossman '608 does not anticipate claims 1-5 and 7-14 and Applicants request that the rejection under 35 U.S.C. §102(e) be reconsidered and withdrawn.

Rejection Under 35 U.S.C. §103(a)

The Examiner rejected claim 6 under 35 U.S.C. §103(a), for allegedly being obvious over Grossman '608 in view of U.S. Patent No. 5,656,145 (Nguyen). Applicants respectfully traverse this rejection.

To establish a *prima facie* case of obviousness, all of the claim elements must be taught or suggested by the prior art. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir.1991). The present claims include, among other things, that detectable breakdown products and residual nucleotide terminators are eluted before non-extended primers so as not to overlap in elution with primer extension product(s). As stated above, Grossman

'608 does not disclose eluting detectable breakdown products and residual labeled nucleotide terminators before non-extended primers so as not to overlap in elution with primer extension product(s). Moreover, Grossman '608 does not address the problem caused by interfering signals between labeled primer extension products and detectable breakdown products and residual labeled terminator nucleotides. In fact, Grossman '608 does not mention detectable breakdown products and residual labeled terminator nucleotides at all.

Like Grossman '608, Nguyen does not disclose, teach or suggest eluting detectable breakdown products and residual nucleotide terminators before non-extended primers so as not to overlap in elution with primer extension product(s). Rather, Nguyen discloses a needle guide that helps the user load a sample into a slab gel (col. 1., lines 28-30). Nguyen says nothing about interfering signals between labeled primer extension products and detectable breakdown products and residual labeled terminator nucleotides. Like Grossman '608, Nguyen does not mention detectable breakdown products and residual labeled terminator nucleotides at all.

Neither Grossman '608 nor Nguyen alone or in combination disclose, teach or suggest the present claims. Further, neither Grossman '608 nor Nguyen recognize the problem addressed by the presently claimed invention e.g., interfering signals between labeled primer extension products, and detectable breakdown products and residual labeled terminators that can elute with extension products and obscure the signal from the labeled extension products. Since neither Grossman '608 nor Nguyen disclose, teach or suggest the present claims, alone or in combination, the claims cannot be considered obvious. Accordingly, Applicants request that the rejection under 35 U.S.C. §103(a) be reconsidered and withdrawn.

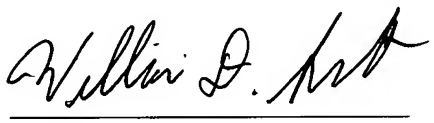
Conclusion

Reconsideration and allowance are respectfully solicited.

Applicants petition the Commissioner for a 2-month extension of time. Enclosed is the required fee. No additional fee is believed to be due with respect to the filing of this amendment. If any additional fees are due, or an overpayment has been made, please charge, or credit, our Deposit Account No. 11-0171 for such sum.

If the Examiner has any questions regarding the present application, the Examiner is cordially invited to contact Applicants' attorney at the telephone number provided.

Respectfully submitted,



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